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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/741,657	12/19/2003	Debbie Law	05882.0177.NPUS01	6189
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HOWREY LLP C/O IP DOCKETING DEPARTMENT 2941 FAIRVIEW PARK DRIVE, SUITE 200 FALLS CHURCH, VA 22042-2924			RAWLINGS, STEPHEN L	
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SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		12/18/2006	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/741,657	LAW ET AL.	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 22 September 2006.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-70 is/are pending in the application.
 4a) Of the above claim(s) 17-70 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-16 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 19 February 2003 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>20041220;20060705</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The election without traverse filed September 22, 2006, is acknowledged and has been entered.

Applicant has elected the invention of Group III, claims 1-16, insofar as the claims are drawn to an antibody that competitively inhibits binding of a GRP64 polypeptide to antibody GPR64-93, or a composition thereof.

2. Claims 1-70 are pending in the application. Claims 17-70 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 22, 2006.
3. Claims 1-16 are currently under prosecution.

Information Disclosure Statement

4. The information disclosures filed July 5, 2006, have been considered. An initialed copy of each is enclosed.

Priority

5. Applicant's claim under 35 USC § 119(e) for benefit of the earlier filing date of U.S. Provisional Application No. 60/435,618, filed December 20, 2002, is acknowledged.

However, claims 1-16 do not properly benefit under 35 U.S.C. § 119 by the earlier filing date of the priority document claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under 35 USC § 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or

provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Furthermore, claims 1-16 do not properly benefit under 35 U.S.C. § 119 by the earlier filing date of U.S. Provisional Application No. 60/435,618 because it does not describe monoclonal antibody GPR64-93, nor does it describe a genus of antibodies that compete for binding to GPR64 with this particular antibody.

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely December 19, 2003.

Specification

6. The disclosure is objected to because the disclosure refers to embedded hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified. Reference to hyperlinks and/or other forms of browser-executable code and to the Internet contents so identified is impermissible and therefore requires deletion.

Examples of such an impermissible disclosures appearing in the application is found in the specification at page 14, line 25, page 15, line 28, and page 17, line 8

The attempt to incorporate essential or non-essential subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP § 608.01(p), paragraph I regarding acceptable incorporation by reference. See 37 CFR § 1.57.

7. The specification is objected to because the use of improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

An example of such improperly demarcated trademarks appearing in the application is Primatized™, which is found in the specification at, e.g., page 12, line 22.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>.

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

Claim 7 is directed to an antibody, which is an antibody fragment that is selected from the group consisting of Fab, Fab', F(ab')₂, Fv fragments, rIgG, diabodies, single chain antibodies, and multispecific antibodies. At page 9, lines 1-5, the specification discloses antibodies, which are antibody fragments with antigen-binding capability are selected from the group consisting of Fab', F(ab')₂, Fab, Fv and rIgG; but the specification does not describe the antibody fragments as inclusive of diabodies, single chain antibodies, and multispecific antibodies.

Appropriate correction is required.

However, it is duly noted that the specification appears to describe antibodies, but not antibody fragments, as inclusive of diabodies, single chain antibodies, and multispecific antibodies, so it is submitted that amending the specification to provide proper antecedent basis for the language of claim 7 would create contradictory or paradoxical disclosures.

Claim Objections

9. Claims 1-16 are objected to because the claims are alternatively drawn to the subject matter of non-elected inventions.

Appropriate correction is required.

10. Claim 5 is objected to because it should properly depend from claim 3, rather than from claim 4, because claim 4 recites the cytotoxic agent is selected from a group including, but not limited to auristatin. Ricin A chain, for example, is not auristatin, so if the cytotoxic agent to which claim 4 is directed is ricin A chain, claim 5 would then illogically recite the cytotoxic agent (ricin A chain, in this example) is auristatin.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 3-5 are indefinite because claim 3 recites, "the effector moiety", where the limitation does not find antecedent basis in the preceding claim (i.e., claim 1). Accordingly, the claims fail to delineate the metes and bounds of the subject matter that Applicant regards as the invention with the necessary clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, so as to permit the skilled artisan to know or determine infringing subject matter.

(b) Claims 1-16 are indefinite for the following reason:

Claims 1-16, which are directed to a genus of antibodies (inclusive of antibody fragments), which compete for binding to a GPR64 polypeptide with an antibody designated "GPR64-93".

The term "GPR64-93" is not expressly defined in the specification as meaning any one particular antibody. It is thus broadly, but reasonably interpreted as meaning any antibody that has the same epitope binding specificity as the monoclonal antibody designated "GPR64-93" and "OAM6#93", which is produced by the hybridoma deposited under ATCC accession number PTA-5704; see, e.g., the table at page 52 of the specification.

Accordingly, the claims are indefinite because, although the specification describes deposited hybridomas that produce a monoclonal antibody designated "GPR64-93", the claims appear directed to a *plurality* of monoclonal antibodies, which are commonly designated "GPR64-93", and which are not necessarily the monoclonal antibody produced by the deposited hybridoma having ATCC accession number PTA-5704.

Use of such laboratory designations as the sole means of identifying the antibodies to which the claims are directed renders the claims indefinite because different laboratories may use the same designations to define completely distinct hybridomas and/or the antibodies produced by hybridomas.

Therefore, because the use of such designations as descriptors of the antibodies renders the claims subject to ambiguous interpretation, the metes and bounds of the subject matter that is regarded as the invention cannot be determined the requisite degree of clarity and particularity to permit the skilled artisan to know or determine

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infringing subject matter, so as to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

Accordingly, it is suggested that the claims be amended to include the depository accession number of the hybridoma producing the one or more antibodies designated "GPR64-93" to which the claims are directed because a depository accession number uniquely identifies a deposited hybridoma, so as to unambiguously define the monoclonal antibody to which a claim is directed.

(c) Claims 1-16 are indefinite for the following reason:

Claim 1 recites, "that competitively inhibits binding of a GPR64 polypeptide" to an antibody designated "GPR64-93".

The term "competition" is defined, for example, by Stedman's Online Medical Dictionary, 27th Edition as meaning: "The process by which the activity or presence of one substance interferes with, or suppresses, the activity of another substance with similar affinities" (Copyright © 2006 Lippincott Williams & Wilkins). Given this definition, the claims are directed to antibodies that interfere with, or suppress binding of an antibody designated "GPR64-93" to a GPR64 polypeptide.

This interpretation is not inconsistent with the specification, since at paragraph [0116] of the published application, the specification discloses: "A first antibody is considered to competitively inhibit binding of a second antibody, if binding of the second antibody to the antigen is reduced by at least 30%, usually at least about 40%, 50%, 60% or 75%, and often by at least about 90%, in the presence of the first antibody", when using any of several assays described therein.

Accordingly, it is evident that the degree to which the claimed antibody "competes" for binding to a GPR64 polypeptide with an antibody designated "GPR64-93" may vary; furthermore, the methodology used to make the determination, and the conditions under which that determination is made, may vary substantially.

Thus, while one may know how to determine whether an antibody "competes" with an antibody designated "GPR64-93", because the degree to which an antibody competes with another antibody is a relative or subjective expression, and the requisite degree to which the claimed antibody competes with the antibody designated "GPR64-

93" is not limited, the metes and bounds of the subject matter encompassed by the claims is expected to vary.

In addition, according to the above-mentioned disclosure of suitable assays, it is evident that one might determine whether an antibody "competes" for binding to a GPR64 polypeptide with an antibody designated "GPR64-93" by measuring the percentage of binding of a detectably labeled antibody in the presence of an unlabeled (i.e., "cold") antibody. As such, it is recognized that the degree of binding of an antibody, which is observed in such competitive binding assays, will depend upon the concentration of the detectably labeled antibody and the unlabeled competing antibody. Typically, the higher the concentration of the unlabeled competitor, the lower the percentage of binding of the labeled antibody. So, at *high enough* concentrations, any antibody might be deemed capable of "competing" for binding to an antigen with any other antibody, regardless of whether or not the different antibodies bind to the same, or even overlapping epitopes.

George et al. (*Circulation*. 1998; **97**: 900-906), for example, describes different antibodies, which do not bind to the same epitope of an antigen, but are nevertheless capable of competing with one another for binding to the antigen; see entire document (e.g., page 903, paragraph bridging columns 1 and 2). More particularly, George et al. describes three antibodies, which bind decidedly different, non-cross-reactive epitopes on β 2GPI; yet, George et al. teaches each is able to "compete" to some extent with any of the others for binding to the antigen (page 903, paragraph bridging columns 1 and 2). For example, George et al. teaches monoclonal antibody ILA-4 competed with itself for binding to the antigen (% inhibition = $90 \pm 11\%$ at competitor antibody concentrations of 30 μ g/ml), but George et al. discloses, despite its binding a non-overlapping epitope, monoclonal antibody ILA-1 also "competed", albeit perhaps unsubstantially with monoclonal antibody ILA-4 for binding to the antigen (% inhibition = $9 \pm 4\%$).

Accordingly, George et al. illustrates the capricious and arbitrary nature of determinations that different antibodies bind to the same or different epitopes, which are based upon the results of competitive binding assays, such as the assay exemplified in

the specification at page 50. Although each of the described antibodies “competed” to a measurable extent with the other antibodies for binding to the antigen, George et al. nevertheless concludes “no competition was achieved”, and the antibodies bind distinct, non-overlapping epitopes.

Therefore, the claims are *not* unambiguously interpreted, as it cannot be determined whether the antibody to which the claims are directed is an antibody that merely inhibits, but does not abrogate the interaction between the antibody designated “GPR64-93” and a “GPR64 polypeptide”. Moreover, if the claimed antibody merely inhibits binding of the antibody designated “GPR64-93” to the “GPR64 polypeptide”, it cannot be determined to what requisite extent the claimed antibody must “competitively inhibit” binding of the polypeptide to the antibody.

Finally, as explained above in subsection (b) of this rejection, the claims are not necessarily limited to the monoclonal antibody produced by the deposited hybridoma, as they are instead more broadly directed to any of a plurality of antibodies that have the same epitope binding specificity as the monoclonal antibody designated “GPR64-93” and “OAM6#93”, which is produced by the hybridoma deposited under ATCC accession number PTA-5704. Pointedly, different members of such a plurality of antibodies do not necessarily bind a GPR64 polypeptide with the same affinity or avidity as the monoclonal antibodies produced by the deposited hybridoma. For example, a humanized “GPR64-93” antibody may have a substantially different binding affinity than the murine monoclonal antibody produced by the deposited hybridoma. Therefore, presuming the concentration of the antibody is not altered, depending upon the affinity and avidity that characterizes any given antibody’s ability to bind an antigen, the claimed antibody is expected to more or less “competitively inhibit” binding of the antibody designated “GPR64-93” to the “GPR64 polypeptide”, so that the metes and bounds of the subject matter encompassed by the claims may vary substantially.

For these reasons, it is submitted that the claims fail to satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph, as they do not delineate the claimed subject matter with the requisite degree of clarity and particularity to permit the skilled artisan to know or determine infringing subject matter.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using monoclonal antibody "GPR64-93"**, which is produced by the hybridoma deposited under ATCC accession number PTA-5704, or a composition thereof, a chimeric or partially or fully humanized version of said monoclonal antibody, which retains the ability to specifically bind to the polypeptide of SEQ ID NO: 2, an immunoconjugate comprising said antibody or chimeric or partially or fully humanized version thereof, which is conjugated to an effector moiety selected from the group consisting of a fluorescent label, a radioisotope, and a cytotoxic agent, *provided the deposit requirements, as further explained below, are first met, does not reasonably provide enablement for making and using an antibody that competitively inhibits binding of a GPR64 polypeptide to an antibody designated "GPR64-93", nor for making and using a conjugate thereof, a fragment thereof, or a composition thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.*

MPEP § 2164.01 states:

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and./or unreasonable experimentation.

(a) The claims are directed to a genus of antibodies that competitively inhibit binding of an antibody to any member of a genus of structurally and functionally varying polypeptides, which includes but is not limited to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

To make the claimed antibodies, one would necessarily have to have the "GPR64 polypeptides", because for the most part antibodies are made by immunizing an animal capable of producing antibodies against an antigen with an immunogenic composition comprising the antigen (e.g. the "GPR64 polypeptide").

The claims are necessarily directed to only those "GPR64 polypeptides" that bind an antibody designated "GPR64-93", so as to be capable of competitively inhibiting binding of an antibody designated GPR64-93 to the "GPR64 polypeptide", and although the specification teaches a "GPR64 polypeptide" comprising the amino acid sequence of SEQ ID NO: 2, it fails to describe with any of the requisite particularity the other "GPR64 polypeptides" to which the claims are directed. Moreover, although the specification describes the polypeptide of SEQ ID NO: 2, it fails to teach which other "GPR64 polypeptides" bind to an antibody designated "GPR64-93", such as the

monoclonal antibody produced by the hybridoma deposited under ATCC accession number PTA-5704.

Consequently, the disclosure would not suffice to enable the skilled artisan to make the “GPR64 polypeptides”, which must be acquired to produce the claimed antibodies; as such, the claimed invention could not be made without undue and/or unreasonable experimentation.

Furthermore, while the specification might provide sufficient guidance and direction to enable the skilled artisan to use an antibody that binds a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, it does not adequately teach how antibodies that competitively inhibit binding of an antibody designated “GPR64-93” to other “GPR64 polypeptides” are used. For example, while the specification teaches an antibody that binds the polypeptide of SEQ ID NO: 2 may be used to inhibit the proliferation of ovarian cancer cells expressing the polypeptide, because the other “GPR64 polypeptides” may not be expressed by ovarian cancer cells, one might not use the claimed invention in this described manner, but would have to elaborate a use for any antibodies that competitively inhibit binding of an antibody designated “GPR64-93” to such other “GPR64 polypeptides”. Any need to elaborate a use for the claimed invention would fall into the realm of undue and/or unreasonable experimentation.

(b) Additionally, the claims are directed to a genus of antibodies or antibody fragments, which do not necessarily bind a GPR64 polypeptide, such as the polypeptide of SEQ ID NO: 2. More particularly, the claimed antibodies or fragments thereof do not necessarily bind to the same epitope as the antibody designated GPR64-93, such as the monoclonal antibody produced by hybridoma deposited under ATCC deposit accession number PTA-5704. Rather, because as evidenced by George et al. (cited *supra*), for example, an antibody need not bind the same epitope of an antigen to “competitively inhibit” binding of another antibody to the antigen, the claims should broadly, but reasonably be interpreted to encompass any antibody, not necessarily an antibody that binds to the same epitope as the monoclonal antibody produced by hybridoma deposited under ATCC deposit accession number PTA-5704, and not

necessarily an antibody that binds to the polypeptide of SEQ ID NO: 2 or any other GPR64 polypeptide.

At paragraphs [0215] and [0216] of the published application, the specification describes one or more of disclosed monoclonal antibodies, including GPR64-81, GPR64-93, and GPR64-101, as binding to one of four distinct epitopes; and it only describes monoclonal antibodies GPR64-18, -61, -62, -65, -95, and -99 as binding to a common epitope. None of other disclosed antibodies, which bind to GPR64, bind to the same epitope as monoclonal antibody GPR64-93.

The claims do not define the extent to which the claimed antibody or antigen binding fragment “competes”, nor do they define the methodology by which such a determination is made, and under what conditions. As evidenced by George et al. (cited supra), for example, at a high enough concentration, or under certain conditions, *any* antibody, but perhaps especially another antibody that binds the same antigen, or more particularly the same epitope recognized by another antibody or an overlapping epitope of the antigen, is expected to “compete” for binding to the antigen with the other antibody.

Nonetheless, regardless of how, and under which conditions, the determination that an antibody or antigen-binding fragment binds to the same or a different epitope, as compared to any member of the recited plurality of antibodies designated “GPR64-93”, is ultimately made, it is necessary to have access to those members to make the claimed invention.

The claims are not necessarily limited to the antibodies or antigen-binding fragments that “compete” for binding to a GPR64 polypeptide with the antibody produced the deposited hybridoma, but are instead more broadly directed to antibodies that compete for binding to the polypeptide with any of a *plurality* of antibodies designated “GPR64-93”.

Although the specification describes the deposit of a hybridoma in accordance with the Budapest Treaty, which produces a mouse monoclonal antibody designated “GPR64-93”, the specification does not teach one to make these antibodies by, for

example, disclosing the entirety of their amino acid sequences or the polynucleotide sequences encoding their amino acid sequences.

Furthermore, although the prior art enables one to make and use many antibodies, which under certain conditions, could demonstrably "compete" for binding to a "GRP64 polypeptide" with any of a plurality of antibodies designated "GPR64-93", Applicant is reminded that to satisfy the enablement requirement, reasonable correlation must exist between the scope of the claims and scope of enablement set forth in the specification. Furthermore, although a specification need not, and preferably omits teachings well known in the prior art, in deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997). Thus, the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify antibodies and antigen-binding fragments thereof, which under certain, albeit unspecified assay conditions "competitively inhibit" binding of an antibody designated "GPR64-93" to a "GPR64 polypeptide"; yet, defining a substance by its principal biological activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See Colbert v. Lofdahl, 21 USPQ2d 1068, 1071 (BPAI 1991).

(c) The claims encompass antibodies or antigen-binding fragments that "compete" for binding to a GPR64 polypeptide with the antibody produced the hybridoma deposited under ATCC accession number PTA-5704.

It is unclear if a cell line (e.g., a hybridoma) that produces an antibody having the exact structural and chemical identity as the mouse monoclonal antibody designated "GPR64-93" is known and publicly available, or can be reproducibly isolated without undue experimentation. Without access to a hybridoma or recombinant cell line

producing the monoclonal antibodies to which the claims are directed, it would not be possible to make and/or use the claimed invention, because it would not be possible to make the antibody, and then use the antibody to determine if the claimed antibody or fragment thereof "competitively inhibits" binding of that antibody to a GPR64 polypeptide.

If the deposit requirements were satisfied, the disclosure would only be sufficient to make the monoclonal antibody produced by the hybridoma deposited under ATCC deposit accession number PTA-5704, as well as an antigen-binding fragment thereof or a chimeric or humanized version thereof.

However, the referral to deposit of a hybridoma producing a murine monoclonal antibody designated "GPR64-93" in the specification at, for example, the table at page 52 is insufficient assurance that all required deposits have been made and all the conditions of MPEP 608.01 (p)(c) are met.

At paragraph [0227] of the published application, the specification discloses: "The deposit will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Protein Design Labs, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon influence of the pertinent U.S. patent [...]".

However, it is submitted that this disclosure does not provide the necessary assurance that that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

Therefore, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

Therefore, in conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

15. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, "Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001). A copy of this publication can be viewed or acquired on the Internet at the following address: <<http://www.gpoaccess.gov/>>.

These guidelines state that rejection of a claim for lack of written description, where the claim recites the language of an original claim should be rare. Nevertheless, these guidelines further state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

With further regard to the proposition that, as *original* claims, the claims themselves provide *in haec verba* support sufficient to satisfy the written description requirement, the Federal Circuit has explained that *in ipsis verbis* support for the claims in the specification does not *per se* establish compliance with the written description requirement:

Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). See also: *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, an original claim may provide written description for itself, but it must still be an adequate written description, *which establishes that the inventor was in possession of the invention*.

In this instance, the claims are directed to a genus of antibodies that competitively inhibits binding of a GPR64 polypeptide to an antibody designated GPR64-93.

Notably, the claims are not drawn to the antibody designated GPR64-93 but rather to any other antibody that competes for binding to a member of a genus of "GPR64 polypeptides" with this particular antibody.

According to the disclosure, the genus of "GPR64 polypeptides" includes, but is not necessarily limited to the polypeptide of SEQ ID NO: 2. Moreover, at paragraph

[0061] of the published application¹, the specification defines the term "GPR64" as inclusive of any of the polypeptides encoded by plurality of structurally and functionally disparate nucleic acid molecules, which include those that encode polymorphic variants, allelic variants, mutants, and interspecies homologues of the polypeptide encoded by the nucleotide sequence set forth as SEQ ID NO: 1, and may include any of such nucleic acid molecules comprising a polynucleotide sequence that has greater than about 60% nucleotide sequence identity to a region of SEQ ID NO: 1 as small as about 25 nucleotides. The term "GPR64" is further defined to include any polypeptides that bind polyclonal antibodies raised against an immunogen comprising an amino acid sequence encoded by a nucleotide sequence of SEQ ID NO: 1 or a conservatively modified variant thereof. Additionally, according to this same disclosure, the "GPR64 polypeptide" to which the claims are directed includes, but is not limited to any polypeptide that is encoded by a nucleic acid molecule that specifically hybridizes under stringent hybridization conditions to a nucleic acid sequence of SEQ ID NO: 1, or the complement thereof, or to any conservatively modified variant thereof. The "GPR64 polypeptide" to which the claims are directed includes, but is not limited to any polypeptide comprising an amino acid sequence that has greater than about 60% amino acid sequence identity to a region of an amino acid sequence of SEQ ID NO: 2; and finally, the genus of "GPR64 polypeptides" is described as including both naturally occurring or recombinant forms of any of the above-mentioned polypeptides.

Given the degree to which the structures and functions of the members of the genus of "GPR64" polypeptides may vary, it is submitted that the polypeptide of SEQ ID NO: 2 is not reasonably considered representative of the genus, as a whole, and the skilled artisan could not immediately envision, recognize or distinguish members of this genus from other polypeptides.

Inasmuch as the specification does not particularly describe any other "GPR64 polypeptides", apart from a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, it also does not describe with any of the requisite particularity to satisfy the

¹ U.S. Patent Application Publication No. 2004/0197325 A1.

written description requirement the antibodies that bind to such other "GPR64 polypeptides", including those capable of competing for binding thereto with the antibody designated GPR64-93.

Furthermore, while the specification describes other antibodies that bind to the polypeptide of SEQ ID NO: 2, it does not describe any of these particular antibodies as having the capability of competing for binding to the polypeptide of SEQ ID NO: 2 or any other "GPR64 polypeptide" with the antibody designated GPR64-93.

At paragraphs [0215] and [0216] of the published application, the specification describes one or more of disclosed monoclonal antibodies, including GPR64-81, GPR64-93, and GPR64-101, as binding to one of four distinct epitopes; and it only describes monoclonal antibodies GPR64-18, -61, -62, -65, -95, and -99 as binding to a common epitope.

Accordingly, because none of other disclosed antibodies, which bind to GPR64, bind to the same epitope as monoclonal antibody GPR64-93, it is reasonably concluded that the specification would fail to convey possession of any other antibody that is capable of competing for binding to the polypeptide of SEQ ID NO: 2 or any other GPR64 polypeptide with monoclonal antibody GPR64-93. This conclusion is deemed reasonable since again the specification does not provide any factual showing that would teach or suggest any of the particularly described antibodies are capable of such competition.

Even so, as evidenced by George et al. (cited supra), for example, antibodies need not bind the same epitope, or even an overlapping epitope of an antigen to "compete" with another antibody for binding to the antigen.

Nevertheless, the specification would not reasonably convey Applicant's possession of the claimed invention at the time the application was filed because it does not describe particularly identifying structural and/or functional features, which would permit the skilled artisan to immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus of antibodies or fragments thereof, which bind to epitopes that differ from the epitope recognized by the antibody

designated GPR64-93 but are still capable of competitively inhibiting binding of the antibody designated GPR64-93 to the GPR64 polypeptide.

Having stated this position, however, it is duly noted the specification insufficiently describes members of the genus of antibodies or fragments thereof that bind the same antigenic determinant or epitope of a GPR64 polypeptide, which is recognized by the monoclonal antibody produced by the deposited hybridoma. Moreover, the specification fails to describe reliably predictable means for determining whether an antibody that binds a GPR64 polypeptide binds to the same epitope of the antigen as any other antibody. The competition binding assay that has been disclosed for use in comparing and contrasting the epitopes to which antibodies bind cannot be used to establish with certainty whether two "competing" antibodies bind to the same epitope of an antigen; and furthermore, the conditions under which the assay is to be used to identify the claimed antibodies, which do or do not bind the same epitope, but which nevertheless "compete" with one of the recited monoclonal antibodies have not been described. For these reasons, even if the claims were directed to antibodies binding the same epitope as the epitope recognized by the antibody produced by the deposited hybridoma, the specification would still not reasonably convey to one skilled in the art that Applicant had possession of the claimed invention at the time the application was filed.

Due to the unpredictable nature of the art, where the claimed antibodies are functionally related by their common abilities to "competitively inhibit" binding of an antibody designated GPR64-93 to a GPR64 polypeptide, but unrelated structurally, absent sufficient description of the claimed invention, those that bind particular epitopes of a GPR64 polypeptide (e.g., the polypeptide of SEQ ID NO: 2) cannot be envisioned, recognized or distinguished from other antibodies that also bind this polypeptide, albeit by the recognition of different epitopes. The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Noelle v. Lederman, 69

USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Where the claimed antibodies are functionally related as binding a common epitope of a GPR64 polypeptide (e.g., the polypeptide of SEQ ID NO: 2), whether the antibodies are or are not structurally related, the specification fails to describe the epitope to which the claimed antibodies bind. “[G]eneralized language may not suffice if it does not convey the detailed identity of an invention.” *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes the genus of antibodies that bind any one particular epitope of a GPR64 polypeptide, such as the epitope to which the monoclonal antibody produced by the deposited hybridoma binds, because no one particular epitope of such a GPR64 polypeptide to which such antibodies bind has been described. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Notably the Federal Circuit has recently decided that the description of a fully characterized molecular target of an antibody is sufficient to adequately describe an antibody that binds that target. See *Noelle v. Lederman*, 69 USPQ2d 1508 (CA FC 2004). However, the same court decided that each case involving the issue of written description, “must be decided on its own facts. Thus, the precedential value of cases in this area is extremely limited.” *Vas-Cath*, 935 F.2d at 1562 (quoting *In re Driscoll*, 562 F.2d 1245, 1250 (C.C.P.A. 1977)).

In this instance, the claims are directed to a genus of antibodies that includes, but are not necessarily limited to antibodies that bind to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which, at least in structural terms, is generally considered a fully characterized antigen; however, the difference here is, although the claimed antibodies bind a GPR64 polypeptide, so as to be capable of competitively inhibiting binding of an antibody designated GPR64-93 to the GPR64 polypeptide, they only bind very particular epitopes of the GPR64 polypeptide that recognized by the antibody designated GPR64-93. The epitope to which the monoclonal antibody

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produced by the deposited hybridoma binds has not been described with the requisite degree of particularity however to permit the skilled artisan to recognize those epitopes.

Following the example set by the Federal Circuit in deciding *Noelle v. Lederman*, then, were the claims directed to an antibody that binds a well-characterized antigen, the written description would be met. However, the claims are not directed to an antibody that binds a well-characterized molecular target, but rather to an antibody that binds to a *very discrete part* (*i.e.*, *epitope*) of a GPR64 polypeptide, which has not been characterized and remain cryptic in nature.

The term "epitope", as it is used in the art of immunology, is more generally used in a broader context to mean an "antigenic determinant", or site on the surface of an antigen molecule to which a single immunoglobulin molecule (*e.g.*, antibody) binds; generally an antigen has several or many different antigenic determinants and reacts with antibodies of many different specificities. Stedman's Online Medical Dictionary, 27th Edition, which is available on the Internet at <http://www.stedmans.com/>, for example, defines the term "epitope" as "[t]he simplest form of an antigenic determinant, on a complex antigenic molecule, which can combine with antibody or T cell receptor".

Notably, Greenspan et al. (*Nature Biotechnology*. 1999; 7: 936-937), for example, teaches that defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include any and all residues of an antigen that make contact with the antibody; even contacts by residues that are energetically neutral, or even destabilizing to binding are constitutive elements of the epitope. Conversely, Greenspan et al. teaches an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue by another might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically.

Thus, even using a competition binding assay, such as that described in the specification, the skilled artisan cannot recognize or distinguish an antibody that binds the same epitope as another antibody because antibodies that compete with one

another for binding to the same antigen do not necessarily bind the same epitope; rather, an antibody may bind a spatially overlapping epitope and thereby sterically hinder binding of the other ligand to its epitope, or as evidenced by George et al. (cited *supra*), an antibody may bind an epitope that is distant from, and spatially non-overlapping with the epitope of an antigen recognized by the other antibody, and still interfere with binding of the latter to the antigen.

Where the claimed antibodies bind an epitope of a GPR64 polypeptide recognized by the monoclonal antibody produced by the deposited hybridoma or any other antibody designated GPR64-93, it is aptly noted that the Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to bind a particular epitope of a polypeptide, or the ability to "compete" for binding to the polypeptide with another antibody, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1984 (CAFC 2004). Without the antibodies to which the claims are directed, it is impossible to make or use the claimed invention.

In addition, although the skilled artisan could initially screen candidate antibodies to identify those that are possibly encompassed by the claims by performing, for example, a competitive binding assay, and then empirically determine whether the selected antibodies bind to the same epitope recognized by one of the recited monoclonal antibodies, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating (or identifying) it.

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

"Guidelines" (cited *supra*) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of antibodies, which vary both structurally and functionally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was

complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. Claims 1, 2, 6-12, 15, and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication No. 2006/0069239 A1, as evidenced by Kirchhoff et al. (*Mol. Cell. Endocrinol.* 2006; **250**: 43-48) and George et al. (*Circulation*. 1998; **97**: 900-906).

U.S. Patent Application Publication No. 2006/0069239 A1 (Kirchhoff et al.) teaches antibodies that bind HE6 (GPR64); see entire document (e.g., paragraphs [0047], [0061], and [0139]). Kirchhoff et al. teaches fragments of such antibodies (e.g., Fab); see, e.g., paragraph [0139]. Kirchhoff et al. teaches the antibodies are chimeric, or partially or fully humanized; see, e.g., paragraph [0139]. Kirchhoff et al. teaches the antibodies are single chain antibodies; see, e.g., paragraph [0139]. Kirchhoff et al. teaches the antibodies are detectably labeled; see, e.g., paragraph [0140]. Kirchhoff et al. teaches the antibodies are formulated as pharmaceutical compositions comprising one or more conventional pharmaceutically acceptable carriers; see, e.g., paragraph [0170].

As evidenced by Kirchhoff et al., HE6 and GPR64 are used to identify the same protein; see entire document (e.g., the abstract; page 43, column 1).

Inasmuch as the effector moiety of claim 2 is, according to claim 3, fluorescent or radioactive, the effector moiety is a detectable label.

Kirchhoff et al. does not expressly teach the disclosed antibody “competitively inhibits” binding of an antibody designated GPR64-93 to a GPR64 polypeptide. Nevertheless, the antibodies disclosed by the prior art are polyclonal; and polyclonal antibodies raised against HE6 (GPR64) bind a plurality of epitopes of the polypeptide, and are reasonably expected to comprise one or more species of antibody that bind to the same epitopes as an antibody designated GPR64-93, which thereby are capable of “competitively inhibiting” binding of the antibody designated GPR64-93 to the polypeptide.

Additionally, as evidenced by George et al. (cited *supra*), an antibody need not bind to the same epitope of an antigen as another antibody to measurably “compete” for binding to the antigen with the other antibody. Thus, at a high enough concentration, or under certain conditions, *any* antibody, including an antibody that binds to a different epitope of an antigen than the epitope recognized by another antibody that binds the antigen is expected to “competitively inhibit” binding of the other antibody to the antigen. Neither the claims nor the disclosure delineate the conditions under which such a determination was made. Moreover, as thoroughly explained above in the rejections of claims under 35 U.S.C. § 112, first and second paragraphs, the claims do not define the extent to which the claimed antibody or antigen binding fragment “competes”, nor do they define the methodology by which such a determination is made, and under what conditions.

Therefore, absent a showing of any difference, the polyclonal and/or monoclonal antibodies disclosed by Kirchhoff et al. are deemed the same as the claimed antibodies and antigen binding fragments thereof. Notably, the Office does not have the facilities for examining and comparing Applicant’s product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the antibodies and antigen binding fragments thereof. In the absence of evidence to the contrary, the burden is upon the

applicant to prove that the antibody disclosed by the prior art differs from the claimed antibody.

Conclusion

18. No claim is allowed.

19. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Obermann et al. (*Mol. Reprod. Dev.* 2003 Jan; **64** (1): 13-26) teaches polyclonal antibodies that bind peptide fragments of HE6 (GPR64); see, e.g., page 15. U.S. Patent Application Publication No. 2003/0138793 A1 teaches the identification of GPR64 as a marker of ovarian cancer (see, e.g., paragraph [0163]). Osterhoff et al. (*DNA Cell Biol.* 1997; **16** (4): 379-389) teaches cloning the mRNA encoding HE6 and its expression in various tissues (see, e.g., the abstract; and page 381, Figure 1). Bhaskar et al. (*Cancer Res.* 2003 Oct 1; **63**: 6387-6394) teaches the up-regulation of a tumor associated antigen allows targeted drug delivery using an immunoconjugate.

Other art made of record, which is also considered pertinent to Applicant's disclosure, is Gottwald et al. (*Mol. Cell. Endocrinol.* 2006; **250**: 49-57), teaching the expression of HE6 by a large variety of normal and cancerous tissues (see, e.g., page 54, Figure 2).

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
December 11, 2006